

IN THE CLAIMS:

Applicants, pursuant to 37 C.F.R. § 1.121, submit the following amendments to the claims:

1. (Currently amended) A method for detecting the presence ~~or absence~~ of a ~~diseased condition~~ cellular proliferative disease in a tissue, cell type or organ of ~~a human-an individual~~, comprising:

obtaining a bodily fluid sample from ~~a human-an individual~~;
determining an amount or presence of free floating DNA that originates from a particular tissue, cell type or organ in the sample comprising analysing for a DNA methylation pattern that is characteristic for the particular tissue, cell type or organ; and

determining the presence ~~or absence~~ of a ~~diseased condition~~ cell proliferative disease based on the amount or presence of free floating DNA that originates from the particular tissue, cell type or organ.

2. (Currently amended) A method for detecting the presence ~~or absence~~ of a ~~diseased condition~~ cell proliferative disease in a tissue, cell type or organ of ~~an~~ a human individual, comprising:

obtaining a bodily fluid sample from an individual;
determining an amount of total free floating DNA in the sample;
determining an amount of free floating DNA that originates from a particular tissue, cell type or organ in the sample comprising analysing for a DNA methylation pattern that is characteristic for the tissue, cell type or organ; and

determining the presence ~~or absence~~ of a ~~diseased condition~~ cell proliferative disease based on the total amount of free floating DNA and the fraction of free floating DNA that originates from the tissue, cell type or organ.

3. (Currently amended) The method of any one of claims 1 and 2, wherein the sample is treated ~~conditioned~~ before the amount or presence of free floating DNA is determined.

4. (Currently amended) The method of claim 3, wherein the sample is treated ~~conditioned~~ by at least one centrifugation, filtering, heating, cooling, concentration and chemical

treatment.

5. (Canceled) ~~The method of any one of claims 1 and 2, wherein determining the amount or presence of DNA originating from the tissue, cell type or comprises analysing for a DNA methylation pattern that is characteristic for the tissue, cell type or organ.~~

6. (Currently amended) The method of ~~claim 5~~ any one of claims 1 and 2, wherein the methylation pattern is characteristic for the particular tissue, cell type or organ and not found in other tissues, cell types or organs involved in the ~~diseased condition~~ cell proliferative disease of interest.

7. (Canceled) ~~The method of claim 5, wherein the diseased condition is at least one from the group consisting of a cell proliferative and a neoplastic disease.~~

8. (Currently amended) The method of ~~claim 5~~ any one of claims 1 and 2, wherein the sample comprises at least one bodily fluid selected from the group consisting of whole blood, blood plasma, blood serum, urine, sputum, ejaculate, semen, tears, sweat, saliva, lymph fluid, bronchial lavage, pleural effusion, peritoneal fluid, meningeal fluid, amniotic fluid, glandular fluid, fine needle aspirates, nipple aspirate fluid, spinal fluid, conjunctival fluid, vaginal fluid, duodenal juice, pancreatic juice, bile and cerebrospinal fluid.

9. (Currently amended) The method of ~~claim 5~~ any one of claims 1 and 2, wherein determining the methylation pattern comprises subjecting the DNA to a chemical or enzymatic treatment that converts all unmethylated cytosines in the DNA into uracil but leaves position 5-methylated cytosines unmodified.

10. (Currently amended) A method for detecting the presence ~~or absence~~ of a ~~diseased condition~~ cell proliferative disease in a particular tissue, cell type or organ in a human individual, comprising:

obtaining a bodily fluid sample;

determining an amount or presence of free floating DNA that exhibits a DNA

methylation pattern characteristic of a particular tissue, cell type or organ;

determining whether there is an ~~abnormal~~ increased level of free floating DNA that originates from the tissue, cell type or organ; and

determining a presence ~~or absence~~ of a ~~diseased condition~~ cell proliferative disease associated with said tissue, cell type or organ, based on the presence ~~or absence, respectively,~~ of such an ~~abnormal~~ increased level of free floating DNA.

11. (Currently amended) A method for detecting the presence ~~or absence~~ of a ~~diseased condition~~ cell proliferative disease in a specific tissue, cell type or organ in a human individual, comprising:

obtaining a bodily fluid sample;

detecting an amount of total free floating DNA in the sample;

determining an amount of free floating DNA that originates from a specific tissue, cell type or organ by determining an amount of free floating DNA that exhibits a DNA methylation pattern characteristic of a tissue-, cell type- or organ;

determining the fraction of total free floating DNA that originates from the specific tissue, cell type or organ;

determining whether an increased~~abnormal~~ level of free floating DNA that originates from the specific tissue, cell type or organ is present; and

determining the presence ~~or absence~~ of a ~~diseased condition~~ cell proliferative disease associated with said tissue, cell type or organ, based on the presence ~~or absence, respectively,~~ of such an ~~abnormal~~ increased level of free floating DNA.

12. (Currently amended) A method for determining the fraction of total free floating DNA in a bodily fluid that originates from a specific tissue, cell type or organ in a human individual, comprising:

obtaining a bodily fluid sample;

conditioning the sample to provide for binding of total free floating DNA to a surface;

binding an amount of the total free floating DNA to the surface;

detecting an amount of total free floating DNA by measuring the amount of DNA bound to the surface;

subjecting the surface comprising the bound DNA to at least one of a chemical and enzymatic treatment that converts all unmethylated cytosines in the DNA into uracil but leaves position-5 methylated cytosines unmodified;

amplifying the treated DNA;

analysing several methylation-specific positions in the treated DNA, and thereby determining an amount of DNA that exhibits a tissue, cell type or organ-characteristic DNA methylation pattern;~~and~~

~~determining the fraction of total free floating DNA that originates from the specific tissue, cell type or organ; and~~

comparing the amount of DNA that exhibits a tissue, cell type or organ-characteristic DNA methylation pattern to the amount of detected total free floating DNA, thereby determining the fraction of free floating DNA that originates from the specific tissue, cell type or organ in the total free floating DNA.

13. (Currently amended) The method of claim 12, further comprising:

determining whether an ~~increased~~abnormal level of free floating DNA that originates from the specific tissue, cell type or organ is present; and

determining the presence ~~or absence~~ of a ~~diseased condition~~ cell proliferative disease associated with said tissue, cell type or organ, based on the presence ~~or absence, respectively,~~ of such an ~~abnormal~~ increased level of free floating DNA.

14. (Previously presented) The method of any one of claims 1, 2, 10, 11, 12 and 13, wherein measuring the total amount of free floating DNA comprises use of at least one means selected from the group consisting of: intercalating fluorescent dyes or other dyes exhibiting changing fluorescence properties upon binding to DNA; hybridisation to DNA specific oligonucleotide or PNA oligomer probes; real time PCR assays; real time amplification procedures; UV-Vis absorbance; and amplification procedures with subsequent determination of the amount of product amplificate formed.

15. (Withdrawn) A kit for determining the total amount of free floating DNA in serum, comprising:

a surface suitable to bind free floating DNA of a sample of bodily fluid;
means for detecting an amount of DNA bound to the surface;
reagents suitable to chemically or enzymatically modify the surface bound DNA to convert all unmethylated cytosines in the DNA into uracil but leave position-5 methylated cytosines unmodified;
a container suitable to host the surface and said reagents; and
means to control and adjust the temperature in the container.